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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,841	07/09/2007	**Charlie D. Chen**	30435159USWO	8702

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
10/27/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,841	CHEN ET AL.	
	Examiner	Art Unit	
	FRANK W. LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9,12-15,18-20 and 61-68* is/are pending in the application.

4a) Of the above claim(s) *18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9,12-15 and 61-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 June 2010* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/6/2007 and 8/30/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group IA, claims 1-4, 9, 12-15 and 61-68 and a hypothetical protein having the Gene bank accession number AF052186 in the reply filed on August 18, 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-4, 9, 12-15, and 61- 68 will be examined.

Drawings

2. Some bands in Figures 1D, 2A to 2C, 3A to 3C, 4C, 5A, 5B, 6, and 7B are unclear. Applicant is required to submit new drawings for Figures 1D, 2A to 2C, 3A to 3C, 4C, 5A, 5B, 6, and 7B. No new matter may be introduced in the required drawing. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d).

Specification

3. The disclosure is objected to because of the following informality: although applicant claims priority for PCT/US04/42258 and US provisional application 60/530,101 in Oath and Declaration, there is no PCT/US04/42258 and US provisional application 60/530,101 in the first paragraph of the specification, applicant may need to add PCT/US04/42258 and US provisional application 60/530,101 in the first paragraph of the specification.

Appropriate correction is required.

Claim Objections

4. Claim 14 is objected to because of the following informality: "insulin-like growth factor binding protein 2 or IGFBP2" should be "insulin-like growth factor binding protein 2 (IGFBP2)".

5. Claim 63 is objected to because of the following informalities: (1) "PTEN tumor suppressor" in line 1 should be "PTEN tumor suppressor gene"; and (2) "profiling PTEN the human tissue specimen" in step (c) should be "profiling PTEN in the human tissue specimen".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Enablement

Claims 1-4, 9, 12-15, and 61- 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the

quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a method of profiling a tumor/cancer in a human tissue specimen, a method of profiling PTEN tumor suppressor gene in a human tissue specimen, and a method of assessing PTEN tumor suppressor gene expression in a human cell. The invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.,* 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The Breadth of The Claims

Claims 1-4, 9, 12-15, 61, and 62 encompass a method of profiling a tumor/cancer in a human tissue specimen by measuring quantitatively the levels of one or plurality of products of genes in said tissue specimen including IGFBP 2 gene. Claims 63-66 encompass a method of profiling PTEN tumor suppressor gene in a human tissue specimen by quantitatively measuring levels of the IGFBP 2 mRNA or polypeptide in the tissue specimen. Claims 67 and 68 encompass a method of assessing PTEN tumor suppressor gene expression in a human cell by examining levels of IGFBP 2 expressed in the human cell using an antibody that binds IGFBP2.

Working Examples

The specification provides working examples for: (1) Random Forest Deals Effectively with Microarray Data; (2) Molecular Signature of the PTEN Tumor Suppressor; (3) Elevated

Levels of IGFBP 2 Expression in PTEN Mutant Tumors; (4) Inhibition of IGFBP 2 Expression by PTEN; (5) Functional Role of IGFBP 2 in the PTEN/Akt Signaling; (6) IGFBP 2 is a Surrogate Marker for PTEN; (7) Serum IGFBP 2 can be developed as a Surrogate Marker for PTEN Mutations and Akt Activation; and (8) Potential Downstream Targets of PTEN (see pages 9-13). The specification provides no working example for the methods recited in claims 1-4, 9, 12-15 and 61-68.

The Amount of Direction or Guidance Provided and The State of The Prior Art

Although the specification provides working examples for: (1) Random Forest Deals Effectively with Microarray Data; (2) Molecular Signature of the PTEN Tumor Suppressor; (3) Elevated Levels of IGFBP 2 Expression in PTEN Mutant Tumors; (4) Inhibition of IGFBP 2 Expression by PTEN; (5) Functional Role of IGFBP 2 in the PTEN/Akt Signaling; (6) IGFBP 2 is a Surrogate Marker for PTEN; (7) Serum IGFBP 2 can be developed as a Surrogate Marker for PTEN Mutations and Akt Activation; and (8) Potential Downstream Targets of PTEN (see pages 9-13), the specification does not provide a guidance to show that the methods recited in claims 1-4, 9, 12-15 and 61-68 can be performed. Furthermore, there is no experimental condition and/or experimental data in the specification to support the claimed invention. During the process of the prior art search, the examiner has not found any 102 type of prior art which is related to the methods recited in claims 1-4, 9, 12-15 and 61-68.

Level of Skill in The Art, The Unpredictability of The Art, and The Quantity of Experimentation Necessary

While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the methods recited in claims 1-4, 9, 12-15 and 61-68 can be performed.

First, although claim 1 requires assessing PTEN tumor suppressor gene mutations, deletions, aberrant or absent PTEN mRNA or PTEN protein, in view of claim 1, it is unclear how PTEN tumor suppressor gene mutations, deletions, aberrant or absent PTEN mRNA or PTEN protein are correlate with the quantitative levels of the said products of genes from step 1 (b) and how to assess PTEN tumor suppressor gene mutations, deletions, aberrant or absent PTEN mRNA or PTEN protein from the quantitative levels of the said products of genes from step 1 (b) as recited in claims 1-4, 9, and 12-15. Furthermore, although claim 14 requires that said reagent is an antibody against IGFBP 2, in view of claims 1 and 14, it is unclear how PTEN tumor suppressor gene mutations, deletions, aberrant or absent PTEN mRNA or PTEN protein are correlate with the quantitative levels of the said products of genes from step 1 (b) and how to assess PTEN tumor suppressor gene mutations, deletions, aberrant or absent PTEN mRNA or PTEN protein from the quantitative levels of the said products of genes from step 1 (b) as recited in claim 14 when said reagent is an antibody against IGFBP 2. In addition, in view of claims 61 and 62, it is unclear that, in which situation, observing levels of IGFBP 2 polypeptide in the tissue specimen can be used to assess said loss of PTEN mRNA or protein.

Second, although claim 63 requires assessing PTEN tumor suppressor gene mutations, deletions, aberrant or absent PTEN mRNA or PTEN protein, in view of claim 63, it is unclear how PTEN tumor suppressor gene mutations, deletions, aberrant or absent PTEN mRNA or PTEN protein are correlate with the levels of the IGFBP2 mRNA or polypeptides observed in

step (b) and how to assess PTEN tumor suppressor gene mutations, deletions, aberrant or absent PTEN mRNA or PTEN protein based on the levels of the IGFBP2 mRNA or polypeptides observed in step (b) as recited in claims 63, 64, and 66. Furthermore, although the specification shows that some mutants of human advanced prostate cancer xenografts and human glioblastomas having no PTEN expression have a high level of IGFBP2 proteins and some wildtypes of human advanced prostate cancer xenografts and human glioblastomas having high PTEN expression have no IGFBP2 protein (see Examples 2 and 3 in pages 9-11 and Table 1 in page 15), the specification does not teach that 3 fold increased IGFBP 2 polypeptide expression in the human cell correlates with 3 fold decreased PTEN mRNA or protein expression in the human cell and 3 fold decreased IGFBP 2 polypeptide expression in the human cell correlates with 3 fold increased PTEN mRNA or protein expression in the human cell as recited in claim 65. In addition, the specification teaches that, in some case (see the sample #429 in Examples 2 and 3 in pages 9-11 and Table 1 in page 15), increased IGFBP 2 polypeptide expression in the human cell does not correlate with decreased PTEN mRNA or protein expression in the human cell so that PTEN in the human tissue specimen cannot be profiled using the levels of the IGFBP2 mRNA or polypeptides observed in step (b) as recited in claim 65.

Third, although the specification shows that some mutants of human advanced prostate cancer xenografts and human glioblastomas having no PTEN expression have high level of IGFBP 2 proteins and some wildtypes of advanced prostate cancer xenografts and glioblastomas having high PTEN expression have no IGFBP2 proteins (see Examples 2 and 3 in pages 9-11 and Table 1 in page 15), the specification does not teach that upregulation of IGFBP2 polypeptide expression in the human cell correlates with 3 fold decreased PTEN mRNA or

protein expression in the human cell as recited in claim 67 and 68. Furthermore, the specification teaches that, in some case (see the sample #429 in Examples 2 and 3 in pages 9-11 and Table 1 in page 15), upregulation of IGFBP2 polypeptide expression in the human cell does not correlate with decreased PTEN mRNA or protein expression in the human cell as recited in claims 67 and 68.

In view of above discussions, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether the method recited in claims 1-4, 9, 12-15, and 61- 68 can be performed.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high, the specification provides one with no guidance that leads one to claimed methods. One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working example related to claimed invention and the no teaching in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-4, 9, 12-15, 61, and 62 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 1 is rejected as vague and indefinite because step (a) does not make sense. Does step (a) mean exposing said human tissue specimen containing one or a plurality of products of genes to one or a plurality of reagents? Please clarify.

Conclusion

11. No claim is allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached on (571)272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /
Primary Examiner, Art Unit 1634
October 25, 2010